UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,883	03/15/2005	Zebulun David Horowitz	PA/4-32458A	5832

1095 7590 10/16/2007

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
JAVANMARD, SAHAR	

ART UNIT	PAPER NUMBER
4133	

MAIL DATE	DELIVERY MODE
10/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,883	HOROWITZ ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *15 March 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office Action is in response to the 371 of PCT/EP03/10239 filed March 15, 2005. Claim 1 is cancelled; amended claims 2-18 are being examined on the merits herein.

Information Disclosure Statement

The references in the IDS have been considered.

Reference entry AA (US Patent 6,255,288) has an incorrect inventor name listed. Carol Loeschorn is the attorney for said patent, the inventor should be listed as Goodship, et al. Appropriate action is required.

Objections

In claim 14, the word "or" has not been deleted. Appropriate correction is required

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-18 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for a method for the

treatment of osteoporosis post-hip fracture, does not reasonably provide enablement for the prevention of subsequent osteoporotic skeletal fractures as recited in these claims.

The instant claims are drawn to a pharmaceutical composition and a method for the prevention of subsequent osteoporotic skeletal fractures. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention:

The instant invention pertains to a method for the prevention of subsequent osteoporotic skeletal fractures.

The state of the prior art:

The skilled artisan would view that the prevention of one or more symptoms of subsequent osteoporotic skeletal fractures totally, absolutely, or permanently, is highly

unlikely, since one cannot guarantee that the subsequent osteoporotic skeletal fractures will always be prevented.

The relative skill of those in the art:

The relative skill of those in the art is very high.

The predictability or lack thereof in the art:

The skilled artisan would view that the treatment to prevent subsequent osteoporotic skeletal fractures, totally, absolutely, or permanently is highly unpredictable.

The amount of direction or guidance presented and the presence or absence of working examples:

In the instant case, no working examples are presented in the specification as filed showing how to prevent subsequent osteoporotic skeletal fractures totally, absolutely, or permanently. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

Genentech, Inc. v. Novo Nordisk, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test the combination in the instant claims whether preventing subsequent osteoporotic skeletal fractures totally, absolutely, or permanently.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 2-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Goodship et al. (US Patent No. 6,255,288 B1).

Goodship teaches methanebisphosphonic acid derivatives, in particular bisphosphonate compounds, which are used clinically to inhibit excessive bone resorption in a variety of diseases such as tumour-induced osteolysis, Paget's disease and osteoporosis (column 1, lines 4-7). Goodship further teaches that it has been found that certain methanebisphosphonic acid derivatives have a highly beneficial effect on fracture repair. These results show that it is possible to use said

methanebisphosphonic acid derivatives to promote a more rapid and stronger fracture healing (column 1, lines 33-40), meeting the limitations of claim 2.

Additionally, Goodship teaches the pharmaceutical compositions may be administered parenterally, such as intravenous or subcutaneous administration (column 9, lines 21-25), meeting the limitations of claim 7.

Goodship also teaches the approximate daily dosage normally to be recommended for a warm-blooded animal weighing approximately 75 kg is of from 0.01 up to 100 mg/kg (i.e., 0.75 mg-7.5 g) (column 9, lines 37-45), meeting the limitations of claim 8.

Goodship teaches a specific bisphosphonate, 3-amino-1-hydroxypropane-1,1-diphosphonic acid, which is administered to the mammal in need thereof, preferably within 7 days after fixation of the fracture (column 9, lines 64- column 10, line 4), meeting the limitations of claims 3-6.

Thus Goodship anticipates the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goodship et al. as applied to claims 2-8 above.

Goodship further teaches administering the active substance as a slow intravenous infusion over a period of one hour (column 3, lines 22-23).

Goodship does not specifically teach intravenous an infusion rate of 15 minutes.

It would have been obvious to one of ordinary skill in the art at the time of the invention to have altered the rate of infusion of the bisphosphonate of one hour as taught by Goodship. Different doses will require varying infusion rates. This variable is deemed a maniputable parameter practiced by a person skilled in the art to obtain the optimum administration regimen.

Claims 9, 10, 12, 13, 17, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodship et al. as applied to claims 2-8 above, and further in view of Reid et al (N Engl J Med).

Goodship is discussed above.

Goodship does not specifically teach zoledronic acid as the bisphosphonate administered in a dosage regimen of about once every six months or once a year. Additionally, Goodship does not teach the administration of an additional daily supplement such as calcium.

Reid teaches that oral bisphosphonates are widely used for treating osteoporosis and have been shown to increase bone mineral density and decrease the rate of fracture (page 653, column 2, lines 1-4). Furthermore Reid teaches zoledronic acid is the most potent bisphosphonate that has been studied in clinical trials to date (page 654, lines 1-2).

Reid further teaches all women in the study received a calcium supplement (1 g per day). At study entry the women were randomly assigned to receive one of six treatment regimens in a double-blind fashion. Three groups received zoledronic acid by intravenous infusion every three months, one group at a dose of 0.25 mg, one at a dose of 0.5 mg, and one at a dose of 1 mg. Two other groups received a total dose of 4 mg of zoledronic acid — one group receiving a single 4-mg infusion at the beginning of the trial and the other group receiving two doses of 2 mg each, one at base line and the other at six months. Thus, there were three groups that received a total dose of 4 mg in

one year. All infusions were 20 ml in volume and were infused over a period of five minutes (page 654, Treatment section).

Thus, it would have been obvious to one of ordinary skill in the art at the time of the invention to have used a bisphosphonate to treat a patient having undergone recent repair of fractures as taught by Goodship and specifically used zolodronic acid as taught by Reid. One would have been motivated to do this because zoledronic is the most potent of the bisphosphonates and is widely used for the treatment of osteoporosis. Furthermore, administering the drug once every six months or once a year is desirable for reasons of increasing patient compliance and convenience.

Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodship et al. as applied to claims 2-13 and 17-18 above, and further in view of Reid et al (New Engl J Med) and Solomon (New Engl J of Med).

Goodship is discussed above.

Reid is discussed above.

Reid does not teach administering vitamin D2 as the daily supplement.

Solomon teaches although potentially devastating, osteoporotic fractures can be prevented. Adequate calcium intake (at least 1200 mg daily for postmenopausal women) and vitamin D intake (400 to 800 IU daily) and further with medications can increase bone density and, more important, reduce the risk of fracture in women with established osteoporosis; they may also benefit women with less severe bone loss

(page 642, column 1, paragraph 2). Further, Solomon teaches that bisphosphonates are the only medications that have been shown in large randomized trails to reduce the risk of hip fracture (column 2, paragraph 1).

Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to have also administered vitamin D2 prior to administration of bisphosphonates because as Solomon teaches, vitamin D2 supplements on a daily basis are common practice for the reduction and prevention of osteoporotic fractures.

Because of the immense problem of morbidity and mortality associated with osteoporotic fractures, pharmaceutical agents and combinations thereof, which serve to improve fracture healing will be a major therapeutic advance.

Conclusion

Claims 2-18 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAHAR JAVANMARD whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY STUCKER can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

SJ

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER
10/15/07